

CLAIMS

(42)

1. Method for targeting cells involved in sclerotic and/or fibrotic diseases in a tissue sample of a subject using a carrier molecule, said carrier molecule being linked to at least one further molecule, said further molecule being selected from the group comprising:
- a cyclic peptide comprising the amino acid sequence RGD
 - a cyclic peptide comprising the amino acid sequence KPT
 - a cyclic peptide comprising the amino acid sequence RKKP
 - a cyclic peptide comprising the amino acid sequence SRNLIDC
2. Method for targeting cells involved in sclerotic and/or fibrotic diseases in a subject using, in a pharmaceutically acceptable amount and form a carrier molecule, said carrier molecule being linked to at least one further molecule, said further molecule being selected from the group comprising:
- a cyclic peptide comprising the amino acid sequence RGD
 - a cyclic peptide comprising the amino acid sequence KPT
 - a cyclic peptide comprising the amino acid sequence RKKP
 - a cyclic peptide comprising the amino acid sequence SRNLIDC
 - a molecule capable of recognising and binding mannose-6-phosphate receptor and at least an amount that is equivalent to at least 10 molecules capable of recognising and capable of binding mannose-6-phosphate receptor linked to HSA are linked to the carrier molecule.
3. Method according to claim 1 or 2 wherein the cells comprise at least one target receptor specific for Hepatic Stellate Cells (HSC) or a receptor that is upregulated on HSC during disease.

4. Method according to any of claims 1-3 wherein the cells comprise at least one target receptor selected from the group of PDGF receptor, collagen type VI receptor, cytokine receptor(s) such as TGF β , TNF α and interleukin 1 β .
5. Method according to any of the claims, wherein the carrier molecule comprises additional drugs or chemicals linked thereto.
6. Method according to any of the preceeding claims, wherein the carrier molecule comprises a diagnostic marker attached thereto.
7. Method according to any of the preceeding claims wherein the cells involved in a sclerotic and/or a fibrotic disease are cells involved in a disease selected from the group consisting of liver fibrosis, in particular cirrhosis, kidney fibrosis, in particular glomerulosclerosis and interstitial fibrosis, lung fibrosis, atherosclerosis and chronic or acute inflammatory processes such as rheumatoid arthritis, Crohns disease, colitis ulcerosa, glomerulonephritis, sepsis and tumor-cell proliferation associated pathology, fibroblast proliferation associated pathology, endothelial cell proliferation associated pathology and osteoblast proliferation associated pathology.
8. Compound for use in a method according to claim 1 or 2 said compound being a carrier molecule linked to at least 10 molecules capable of recognising and capable of binding mannose-6-phosphate receptor are linked to the carrier molecule, with the proviso the compound is not a naturally occurring peptide with terminal mannose-6-phosphate residues, latent tumor growth factor beta, thyroglobulin or a lysosomal protein.
9. Compound according to claim 8 wherein the molecule capable of recognising and capable of binding mannose-6-phosphate receptor is mannose-6-phosphate.
10. Compound for use in a method according to any of the claims 1-7 said compound being a carrier molecule linked to at least one further molecule said further molecule being X*YRGDYX*, wherein X* represents the location of cyclisation and Y represents at least one amino acid or a sequence of amino acids up to a length such that the target receptor binding capacity of the further molecule is retained.

11. Compound according to claim 10 wherein said further molecule is X*GRGDSPX , wherein X* represents the location of cyclisation.
- 5 12. Compound for use in a method according to any of claims 1-7 said compound being a carrier molecule linked to at least one further molecule said further molecule being X*YKPTYX*, wherein X* represents the location of cyclisation and Y represents at least one amino acid or a sequence of amino acids up to a length such that the target receptor binding capacity of the further molecule is retained.
- 10 13. Compound according to claim 12 wherein said further molecule is X*DKPTLX*, wherein X* represents the location of cyclisation.
- 15 14. Compound for use in a method according to any of claims 1-7 said compound being a carrier molecule linked to at least one further molecule said further molecule being X*SRNLIDCX*, wherein X* represents the location of cyclisation.
- 20 15. Compound for use in a method according to any of claims 1-7 said compound being a carrier molecule linked to at least one further molecule said further molecule being X*RKKPX*, wherein X* represents the location of cyclisation.
16. Compound according to any of claims 10-15 wherein X* is a cystein residue.
- 25 17. Compound according to any of claims 10-16 wherein X* represents the location of cyclisation and attachment to the carrier molecule.
18. Compound according to any of the claims 8-17 wherein of the further molecule the cyclic portion of the cyclic peptide comprises multiple receptor binding sequences.
- 30 19. Compound according to any of the claims 8-18 wherein of the further molecule the cyclic portion of the cyclic peptide comprises multiple receptor binding sequences directed at at least two different types of receptors.

20. Compound according to any of the claims 8-19, wherein the further molecule comprises multiple cyclic peptides directed at the same or different types of receptors.
21. Compound according to any of the claims 8-20, wherein the carrier molecule is
5 selected from the group of carrier molecules consisting of proteins, oligo or polypeptides, immunoglobulins or parts thereof, oligonucleotides, disaccharides, polysaccharides, biodegradable synthetic polymers, liposomes, lipid particles, biocompatible polymers in the form of microspheres or nanoparticles, endogenous plasma proteins e.g. albumin, lactoferrin, alkaline phosphatase, superoxide dismutase, alpha2 macroglobulin and
10 fibronectin.
22. Compound according to any of the claims 8-21, wherein the carrier molecule comprises additional drugs or chemicals linked thereto.
- 15 23. Compound according to any of the claims 8-23 wherein the carrier molecule comprises a diagnostic marker attached thereto.
24. Pharmaceutical composition comprising a compound according to any of claims 8-23 as targeting ingredient and one or more pharmaceutically acceptable carriers.
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25. Use of a compound according to claim 8-23 for in vitro diagnosis of a sclerotic and/or fibrotic disease in particular for in vitro diagnosis of a disease selected from the group consisting of liver fibrosis, in particular cirrhosis, kidney fibrosis, in particular glomerulosclerosis and interstitial fibrosis, lung fibrosis, atherosclerosis and chronic or
25 acute inflammatory processes such as rheumatoid arthritis, Crohns disease, colitis ulcerosa, glomerulonephritis, sepsis and tumor-cell proliferation associated pathology, fibroblast proliferation associated pathology, endothelial cell proliferation associated pathology and osteoblast proliferation associated pathology with the provisio the compound *cyclo*[-D-Val-Arg-Gly-Asp-Glu(-εAhx-Tyr-Cys-NH)-] linked to BSA is not
30 used in a cell adhesion assay for endothelial cells.
26. Use of a compound according to claim 8-23 or a pharmaceutical composition according to claim 24 for in vivo diagnosis, prophylaxis and/or therapy of a sclerotic

and/or fibrotic disease in particular for in vitro diagnosis of a disease selected from the group consisting of liver fibrosis, in particular cirrhosis, kidney fibrosis, in particular glomerulosclerosis and interstitial fibrosis, lung fibrosis, atherosclerosis and chronic or acute inflammatory processes such as rheumatoid arthritis, Crohns disease, colitis
5 ulcerosa, glomerulonephritis, sepsis and tumor-cell proliferation associated pathology, fibroblast proliferation associated pathology, endothelial cell proliferation associated pathology and osteoblast proliferation associated pathology.